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60/440,732 17 January 2003 (17.01.2003) **US**
- (71) Applicant (for all designated States except US): **MERCK & CO. INC.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **ASHTON, Wallace, T.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **CALDWELL, Charles, G.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **MATH-VINK, Robert, J.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **OK, Hyun, O.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **REIGLE, Leah, Bitlac** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **WEBER, Ann, E.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (74) Common Representative: **MERCK & CO. INC.**; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
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(54) Title: 3-AMINO-4-PHENYLBUTANOIC ACID DERIVATIVES AS DIPEPTIDYL PEPTIDASE INHIBITORS FOR THE TREATMENT OR PREVENTION OF DIABETES

(57) Abstract: The present invention is directed to 3-amino-4-phenylbutanoic acid derivatives which are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/00763

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A 61K 31/4365; C07D 513/04

US CL : 514/300, 301; 546/113, 114

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/300, 301; 546/113, 114

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database CASPLUS on STN(Columbus, OH, USA), No. 130:168654 'Preparation of N-acylamino acid amide compounds as platelet aggregation inhibitors' Kuroki et al. abstract, (1999)see entire reference and RN 220387-47-3.	1-5, 43-49
X	US 6,265,418 B1 (Kuroki et al.) 24 July 2001, see entire reference especially, columns 30-35 and 61-69 compounds, col. 118 lines 9-15 and col. 188-194 starting material.	1-5, 43-49
Y		1-5, 18-23, 42-49, 51-52
Y	Burger "A guide to the chemical basis of drug design" p.15, (1983), see entire reference	51-52

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

01 February 2005 (01.02.2005)

Date of mailing of the international search report

07 MAR 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Authorized officer

Celia Chang

Facsimile No. (703) 305-3230

Telephone No. 571-272-0679

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/00763

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: Please See Continuation Sheet
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☒
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00763

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general -inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-2, 42-49, 51-52 in part when X is CR1, Y is CR1, Z is S, and claims 3-5 drawn to pyridylthienyl ring compounds.

Group II, claims 1-2, 42-52 in part when two of the X, Y, Z is NR2 or N, and claims 6-10, 30-35 drawn to pyridyldiazole/pyridylimidazole compounds.

Group III, claims 1-2, 42-49, 51-52 in part when one X, Y, Z is NR2 or N, one is CR1, one is O, and claims 11-17, 24-29, drawn to pyridyloxazole/pyridylisoxazole compounds.

Group IV, claims 1-2, 42-52 in part when one X, Y, Z is NR2 or N, one is CR1, one is S, and claims 18-23 drawn to pyridylthiazole/pyridylisothiazole compounds.

Group V, claims 1-2, 42-49, 51-52 in part when X, Y, Z are all N, drawn to pyridyltriazoles.

58 The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

PCT administrative instruction section 206 Annex B(f) Markush Practice (i)(B)(2)(v) says " When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the examiner..."

In the instant case, at least one Markush alternative is not novel because the claims are compounds with position homologs of the prior art compounds (see CA 127:149410, the amino substituent is at the homologous location).

Continuation of Box III Item 3:

3-5, 18-23, and 1-2, 42-4-, 51-52 in part when X-Y-Z forms thienyl, thiazol or isothiazol.

Continuation of B. FIELDS SEARCHED Item 3:

Form PCT/ISA/210 (extra sheet) (January 2004)